

PATENT COOPERATION TREATY

REC'D 04 APR 2005

From the
INTERNATIONAL SEARCHING AUTHORITY

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To:
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

01 APR 2005

FOR FURTHER ACTION

See paragraph 2 below

Applicant's or agent's file reference

07917-251WO1

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US04/38950

19 November 2004 (19.11.2004)

21 November 2003 (21.11.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12Q 1/68; C12N 15/63 and US Cl.: 435/6, 455

Applicant

U. MASSACHUSETTS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/38950

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing
☐ contained in international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/38950

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>7, 9-17</u>	YES
	Claims <u>1-6, 8</u>	NO
Inventive step (IS)	Claims <u>7, 9-17</u>	YES
	Claims <u>1-6, 8</u>	NO
Industrial applicability (IA)	Claims <u>1-17</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by Mansell et al. The intended use of the instant claims ("for use in the treatment of acute pancreatitis") is not given patentable weight in this consideration. Mansell et al disclose THP-1 or HEK 293 cells expressing TLR4 that are treated with the serpin antithrombin III. This treatment blocks NF-kB activation via the TLR4 pathway. See the abstract, second full paragraph, second column, pg. 313, and Fig. 4, pg. 315.

Claim 1 lacks novelty under PCT Article 33(2) as being anticipated by Yoshimura et al. The intended use of the instant claims ("for use in the treatment of acute pancreatitis") is not given patentable weight in this consideration. Yoshimura et al disclose a decrease in TLR4 activity in response to LPS from *P. gingivalis* and *C. ochracea*. This treatment blocks NF-kB activation via the TLR4 pathway. See the abstract, Fig. 1, page 220 and Fig. 3, pg. 221.

Claims 1 and 8 lack novelty under PCT Article 33(2) as being anticipated by Su et al. The intended use of the instant claims ("for use in the treatment of acute pancreatitis") is not given patentable weight in this consideration. Su et al disclose a monoclonal antibody to TLR4 that inhibits LPS-induced TLR4 pathway. See the abstract, paragraph bridging first and second columns page 3498, and Fig. 4, pg. 3499.

Claims 1 and 8 lack novelty under PCT Article 33(2) as being anticipated by Hatakeyama et al. The intended use of the instant claims ("for use in the treatment of acute pancreatitis") is not given patentable weight in this consideration. Hatakeyama et al disclose a monoclonal antibody to TLR4 that inhibits the TLR4 pathway. See the abstract, paragraphs bridging first, second and third columns page 19, and Fig. 5, pg. 19.

Claims 1-6 and 8 lack novelty under PCT Article 33(2) as being anticipated by Arditì et al. The intended use of the instant claims ("for use in the treatment of acute pancreatitis") is not given patentable weight in this consideration. Arditì et al disclose methods for inhibiting the activity of TLR4 using antisense RNA or siRNA molecules that inhibit the expression of TLR4, proteins that compete with TLR4 ligands (such as MD-2), or TLR4 antibodies. See pages 5-8.

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International application No.

PCT/US04/38950

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

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